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Amendment to the Claims

A listing of the claims, with Claims 3-15, 31 and 32 as presently amended and Claims 16-30 and 33-46 as cancelled without prejudice or disclaimer, is presented below.

1. (Original) A method for predicting the binding affinity of a peptide for a major histocompatibility (MHC) class I or class II molecule, comprising the following steps:

a) receiving a representation of a complete or partial three-dimensional structure of an MHC class I or class II molecule,

b) obtaining an ensemble of representations of peptide backbone structures of said peptide, said representations located within the binding site of said MHC molecule,

c) modeling for each peptide backbone structure of said ensemble in relation to said MHC molecule, at least the side-chains of said peptide, thereby obtaining an ensemble of modeled MHC/peptide complexes, and

d) evaluating the binding properties of said peptide for said MHC molecule, comprising at least:

d1) evaluating one or more components of the potential energy of each complex of the ensemble,

d2) evaluating the conformational entropy for the complete ensemble.

2. (Original) A method according to claim 1 wherein said representation of step (a) is obtained from one of the following:

- one or more experimentally determined structures obtained by for example X-ray crystallography, nuclear magnetic resonance spectroscopy, scanning microscopy, or

- one or more models derived from an experimentally determined structure, whereby said experimentally determined structure has a high sequence identity to said MHC molecule.

3. (Presently Amended) A method according to claim 1 ~~or 2~~ wherein said representation of step (b) is generated by a computer modeling method, said method being able to generate multiple energetically favorable backbone configurations in relation to said MHC molecule.

4. (Presently Amended) A method according to claim 1 ~~or 2~~ wherein said representation of step (b) is retrieved from a library of peptide structures pre-oriented in relation to said MHC molecule.

5. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 4~~ wherein a complex within said ensemble of step (c) is obtained from a side-chain placement algorithm.

6. (Presently Amended) A method according to ~~any of~~ claims ~~1 to~~ 5 wherein the side-chain placement of step (c) not only involves placing the side-chains of the peptide itself, but also involves placing at least one side-chain of said MHC molecule that are in contact with said peptide.

7. (Presently Amended) A method according to ~~any of~~ claims 5 ~~1 to 6~~ wherein a complex within said ensemble of step (c) is obtained from a side-chain placement algorithm suited for global side-chain optimization.

8. (Presently Amended) A method according to ~~any of~~ claims 5 ~~to 7~~ wherein the side-chain placement algorithm is a dead-end elimination (DEE) algorithm, characterized in that said DEE algorithm eliminates rotameric conformations on the basis of a mathematical criterion that allows the detection of conformations that are not compatible with the globally optimal conformation.

9. (Presently Amended) A method according to ~~any of~~ claims 5 ~~to 7~~ wherein the side-chain placement algorithm is a FASTER algorithm, said algorithm being characterized by a repeated perturbation, relaxation and evaluation step.

10. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 9~~ wherein the binding affinity of step (d) is represented by a single scoring value for the whole ensemble of MHC/peptide complexes, said scoring value comprising the sum of the conformational entropy for the complete ensemble of MHC/peptide complexes, and the average of the said energetical components of each of the complexes of said ensemble.

11. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 10~~ wherein the binding affinity of step (d) is evaluated for the global complex, thereby accounting for interactions between pairs of residues from the peptide, the MHC molecule and both the peptide and the MHC molecule.

12. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 11~~ wherein the entropical component reflects the overall conformational flexibility of the peptide.

13. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 12~~ wherein the representations of said peptide contained in said library are derived from experimentally determined structures.

14. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 12~~ wherein the representations of said peptide contained in said library are derived from computer-generated structures~~, said structures generated by said computer modeling method of claim 3~~.

15. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 14~~ wherein said peptide comprises one or more non-naturally occurring amino acids.

16-30. (Cancelled).

31. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 30~~ wherein said MHC class I molecule comprises an HLA antigen selected from any of the HLA-A, HLA-B, HLA-C, HLA-E, HLA-F and HLA-G alleles.

32. (Presently Amended) A method according to ~~any of~~ claims 1 ~~to 30~~ wherein said MHC class II molecule comprises an HLA antigen selected from any of the HLA-DR, HLA-DQ and HLA-DP gene products.

33-46. (Cancelled).